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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/626,686	07/25/2003	Seishi Kato	01997.013600.8	2374

45743 7590 01/26/2006

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EXAMINER	
HISSONG, BRUCE D	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 01/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/626,686	KATO ET AL.	
	Examiner	Art Unit	
	Bruce D. Hissong, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) *2-6* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-6* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *7/25/2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *07/25/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Comparison*.

DETAILED ACTION

Formal matters

1. The contents of the instant application, including the claims, specification, abstract, drawings, and oath and declaration, were received on 07/25/2003, and have been entered into the record.

2. Claims 1-6 are currently pending. Claims 2-6 have been withdrawn as being non-elected subject matter; therefore claim 1 is the subject of this Office Action.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claim 1, drawn to a protein, classified in class 514, subclass 2.

II. Claims 2-6, drawn to nucleic acids, vectors, and host cells, classified in class 435, subclass 69.1.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are independent and distinct, each from each other, because they are products which possess characteristic differences in structure and function and each has an independent utility that is distinct for each invention which cannot be exchanged.

The polypeptide of group I and the polynucleotide of group II are patentably distinct for the following reasons: polypeptides, which are composed of amino acids, and polynucleotides, which are composed of purine and pyrimidine units, are structurally distinct molecules; any relationship between a polypeptide and polynucleotide is dependent upon the information provided by the nucleic acid sequence open reading frame as it corresponds to the primary amino acid sequence of the encoded polypeptide. Furthermore, searching the inventions of groups I and II together would impose a serious search burden. In the instant case, the search of the polypeptides and the polynucleotides is not coextensive. The inventions of groups I and II

have a separate status in the art as shown by their different classifications. In cases such as this one where descriptive sequence information is provided, the sequences are searched in appropriate databases. There is also search burden in the non-patent literature. Prior to the concomitant isolation and expression of the sequence of interest there may be journal articles devoted solely to polypeptides which would not have described the polynucleotide. Similarly, there may have been "classical" genetics papers which had no knowledge of the polypeptide, but spoke to the gene. Searching, therefore, is not coextensive. As such, it would be burdensome to search the inventions of groups I and II.

Additionally, groups I and II, are subject to further restriction. It is noted that the claims are drawn to examination of at least one of a number of structurally distinct and non-overlapping polypeptides (Group I, claim 1) or nucleic acid sequences (Group II, claims 3-4). In order to be fully responsive, applicant is required to further restrict one specific amino acid sequence if electing Group I, and one specific nucleic acid sequence if electing Group II. This is NOT an election of species. The claimed polypeptides and nucleic acids are non-overlapping sequences and are structurally distinct chemical compounds, and are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such polypeptide or nucleic acid is presumed to represent an independent and distinct invention, subject to restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141. By statute "[i]f two or more independent and distinct inventions are claimed in one application, the Commissioner may require the application to be restricted to one of the inventions." 35 U.S.C. 121. Pursuant to this statute, the rules provide that "[i]f two or more independent and distinct inventions are claimed in a single application, the examiner in his action shall require the applicant.....to elect that invention to which his claim shall be restricted." 37 CRF 1.142(a). See also 37 CFR 1.141(a). It is noted that search more than one of the claimed patentably distinct polypeptides or nucleic acids represents a serious burden for the office.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

During a telephone conversation with Lawrence Perry on 12/13/2005, a provisional election was made without traverse to prosecute the invention of Group I, claim 1, and SEQ ID NO: 1. Affirmation of this election must be made by applicant in replying to this Office action. Claims 2-6 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Priority

The instant application is a CON of 09/455,258 (ABN), filed on 12/01/1999, which is a 371 of PCT/JP98/02445, filed on 06/03/1998. The Applicants also claim priority to foreign applications JAPAN 9-144948, filed on 06/03/1997. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d), however, a certified copy of JAPAN 9-144948 has not been received at the time of this Office Action. Therefore, the earliest effective filing date has been determined to be 06/03/1998. However, if Applicants do file certified copies of JAPAN 9-144948, with English translation, the priority date will be reconsidered.

Information Disclosure Statement

The information disclosure statement received on 07/25/2003 has been fully considered by the Examiner.

Specification

1. The specification is objected to for improper use of trademarks. The use of the trademark RNasin has been noted in this application (p. 25, line 24). It should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of

trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

2. The specification is objected to for failing to include sequence identifiers. According to 37 CFR 1.821(d) (MPEP § 2422), where the description or claims of a patent application discuss a sequence listing that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the assigned identifier, in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application. Sequences appear on page 22, lines 16-17, and page 33, lines 12-14, and in Tables 4-12 of the specification, as well as in Figure 1, but are not identified by SEQ ID NO as required.

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The title recites DNA; however, due to the election of group I, claim 1, the instant invention in drawn to polypeptides having transmembrane domains. The following title is suggested: Human proteins having transmembrane domains.

Claim Objections

Due to Applicant's election of SEQ ID NO: 1, claim 1 is objected to as being drawn to non-elected subject matter (SEQ ID NO: 2-6). Applicants are requested to cancel non-elected subject matter.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

1. Claim 1 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claim recites "a protein comprising an amino acid sequence

selected from the group consisting of.....", and as written does not show the "hand of man" in the inventive process. The Examiner suggests the claim be amended to recite "an *isolated* protein comprising.....".

2. Claim 1 is rejected under 35 U.S.C. 101 because the claimed invention is not supported by a specific, substantial and credible asserted utility, or a well-established utility. The claim is directed to a protein comprised of SEQ ID NO: 1. However, the invention encompassed by the claim has no apparent or disclosed patentable utility. This rejection is consistent with the current utility guidelines, published 01/05/2001, 66 FR 1092. The instant application has provided a description of a protein defined by SEQ ID NO: 1. However, the instant application does not disclose a specific and substantial biological role of this protein, or its significance. There is no biological activity, phenotype, disease or condition, ligand, binding partner, or any other specific feature that is disclosed as being associated with the protein of SEQ ID NO: 1, other than it is a protein of approximate 42 - 50 kD, possesses a cystatin-like domain, is expressed in liver cells, and has approximately 25% homology to human α-2-HS-glycoprotein (p. 27, line 11 – p. 28, line 2, and p 29, lines 10-20). Without any information as to the specific properties and functions of the protein of SEQ ID NO: 1, the mere identification of the polypeptide is not sufficient to impart any particular utility to the claimed protein. Because significant further research would be required of the skilled artisan to determine how the claimed protein is involved in any activity, the asserted utilities are not substantial. Pages 56-82 of the specification assert the following as utilities for the claimed protein (SEQ ID NO: 1):

1) to determine biological activity in an assay, to raise antibodies, as a tissue marker, and to screen for inhibitors or agonists of ligand binding (p. 57-58)

2) as a nutritional source or supplement (p. 58)

3) as a stimulator of cell proliferation or differentiation (p. 59)

4) as a stimulator or suppressor of immune function (p. 61)

5) as a regulator of hematopoesis (p. 70)

6) as a promoter of tissue growth (p. 72)

7) as a promoter of activin/inhibin activity (p. 76)

8) as a stimulator of chemotactic/chemokinetic activity (p. 77)

9) as a regulator of hemostatic/thrombolytic activity (p. 78)

10) receptor/ligand activity (p. 79)
11) as a promoter of anti-inflammatory activity (p. 80)
12) as a tumor inhibitor (p. 81)

These are discussed below:

1) *to determine biological activity in an assay, to raise antibodies, as a tissue marker, and to screen for inhibitors or agonists of ligand binding.* These asserted utilities are not specific or substantial. Because the same assays can be performed with any polypeptide, the asserted utility is not specific to the claimed protein of SEQ ID NO: 1. The asserted utilities are also not substantial because the specification does not disclose any specific biological activity than can be determined by using the protein of SEQ ID NO: 1. Similarly, the specification does not disclose any specific information about inhibitors or agonists of ligand binding, or even the identification of a ligand for the protein of SEQ ID NO: 1. Furthermore, because any virtually any protein has a specific pattern of tissue distribution, this proposed utility is not specific. Likewise, any polypeptide can be used as an immunogen for the production of antibodies. Because it would take significant further research to determine how to use the protein of SEQ ID NO: 1 in these assays, the asserted utility is not present in a ready-to-use, real-world application, and thus the asserted utilities are not substantial.

2) *as a nutritional source or supplement.* This asserted utility is not specific. Virtually any polypeptide can be used as a nutritional source or supplement depending on the intended recipient cell population. Furthermore, it would require significant further research to determine which cell types/organisms could utilize the protein of SEQ ID NO: 1 as a nutritional source.

3-12) *as a stimulator of cell proliferation or differentiation, stimulator/suppressor of the immune system, regulator of hematopoesis, promoter of tissue growth, promoter of activin/inhibin activity, stimulator of chemotactic/chemokinetic activity, receptor/ligand activity, promoter of anti-inflammatory activity, tumor inhibitor.* These asserted utilities are neither specific nor substantial. Because many proteins possess the activities in the asserted utilities, these utilities are not specific to the protein of SEQ ID NO: 1. Furthermore, the specification does not disclose any information concerning the biological role(s) of the protein encoded by

SEQ ID NO: 1. The mere recitation of relative homology/identity to another protein, in this case 25% homology to α-2-HS-glycoprotein, and the identification of a putative cystatin-like domain, is not sufficient to impart any real-world biological function to the protein. There also is no identification of any natural/biological ligand or receptor for the protein of SEQ ID NO: 1. There is no evidence presented in the specification that the protein of SEQ ID NO: 1 could be used to stimulate, promote, or regulate in any way, any of the biological activities listed above. Although the specification recites numerous diseases that may be treatable with the protein of SEQ ID NO: 1, there is no disclosure of any disease state that is associated with normal or abnormal activity, or expression levels of the protein defined by SEQ ID NO: 1. Additionally, because the ligand or receptor for SEQ ID NO: 1 is unknown, it is not possible to predict which tissues or cell types would be responsive to treatment/stimulation with the protein of SEQ ID NO: 1, and therefore it would not be clear to a skilled artisan how to use the protein of SEQ ID NO: 1 in the treatment of any disease, or in the stimulation, promotion, or regulation of any cellular or physiological process. In summary, significant further research would be required of a skilled artisan to determine *if* the protein of SEQ ID NO: 1 could be used in these asserted utilities, and if so, *how* it could be used. Because these asserted utilities are not present in ready-to-use, real-world applications, these asserted utilities are not substantial.

Claim Rejections - 35 USC § 112, first paragraph - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a substantial, well-established utility. Claim 1 is therefore also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a substantial, well-established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 1 is rejected under 35 U.S.C. 102(e) as being anticipated by Edwards *et al* (US20040110939A1). The claim of the instant application is drawn to a protein comprised of the amino acid sequence defined by SEQ ID NO: 1. Edwards *et al* disclose an amino acid sequence (SEQ ID NO: 425) with 100% identity to the SEQ ID NO: 1 of the instant application (see attached sequence comparison). Therefore, Edwards *et al* anticipates claim 1 of the instant application.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571) 272-3324. The examiner can normally be reached M-F from 8:30am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, Ph.D., can be reached at (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BDH
Art Unit 1646

ROBERT S. LANDSMAN, PH.D
PRIMARY EXAMINER

Sequence Comparison - Seq ID NO: 1

```
RESULT 1
US-09-978-360A-425
; Sequence 425, Application US/09978360A
; Publication No. US20040110939A1
; GENERAL INFORMATION:
;  APPLICANT: Edwards, Jean-Baptiste Dumas Milne
;  APPLICANT:  Duclert, Aymeric
;  APPLICANT:  Bougueleret, Lydie
;  APPLICANT:  Jobert, Severin
;  APPLICANT:  Clusel, Catherine
;  TITLE OF INVENTION: Complementary DNA's Encoding Proteins with Signal
Peptides
;  FILE REFERENCE: 56.US4.CIP
;  CURRENT APPLICATION NUMBER: US/09/978,360A
;  CURRENT FILING DATE:  2001-10-15
;  PRIOR APPLICATION NUMBER: US 60/066,677
;  PRIOR FILING DATE: 1997-11-13
;  PRIOR APPLICATION NUMBER: US 60/069,957
;  PRIOR FILING DATE: 1997-12-17
;  PRIOR APPLICATION NUMBER: US 60/074,121
;  PRIOR FILING DATE: 1998-02-09
;  PRIOR APPLICATION NUMBER: US 60/081,563
;  PRIOR FILING DATE: 1998-04-13
;  PRIOR APPLICATION NUMBER: US 60/096,116
;  PRIOR FILING DATE: 1998-08-10
;  PRIOR APPLICATION NUMBER: US 60/099,273
;  PRIOR FILING DATE: -09-04
;  PRIOR APPLICATION NUMBER: US 09/191,997
;  PRIOR FILING DATE: 1998-11-13
;  PRIOR APPLICATION NUMBER: US 09/215,435
;  PRIOR FILING DATE: 1998-12-17
;  PRIOR APPLICATION NUMBER: PCT/IB98/02122
;  PRIOR FILING DATE: 1998-12-17
;  PRIOR APPLICATION NUMBER: US 09/247,155
;  PRIOR FILING DATE: 1999-02-09
;  Remaining Prior Application data removed - See File Wrapper or PALM.
;  NUMBER OF SEQ ID NOS: 810
;  SOFTWARE: Patent.pm
; SEQ ID NO 425
;   LENGTH: 382
;   TYPE: PRT
;   ORGANISM: Homo Sapiens
;   FEATURE:
;   NAME/KEY: SIGNAL
;   LOCATION: -15..-1
US-09-978-360A-425

  Query Match             100.0%;  Score 2018;  DB 3;  Length 382;
  Best Local Similarity   100.0%;  Pred. No. 1.5e-170;
  Matches  382;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MGLLLPLALCILVLCCGAMSPPQLALNPSALLSRGCNDSDVLAVAGFALRDINKDRKDGY 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MGLLLPLALCILVLCCGAMSPPQLALNPSALLSRGCNDSDVLAVAGFALRDINKDRKDGY 60

Qy         61 VLRLNRVNDAQEYRRGGLGSLFYLTLDVLETDCHVLRKKAWQDCGMRIFFESVYGQCKAI 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 VLRLNRVNDAQEYRRGGLGSLFYLTLDVLETDCHVLRKKAWQDCGMRIFFESVYGQCKAI 120

Qy        121 FYMNNPSRVLYLAAYNCTLRPVSKKKIYMTCPDCPSSIPTDSSNHQVLEAATESLAKYNN 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 FYMNNPSRVLYLAAYNCTLRPVSKKKIYMTCPDCPSSIPTDSSNHQVLEAATESLAKYNN 180
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Sequence Comparison - Seq ID NO: 1

```
Qy      181 ENTSKQYSLFKVTRASSQWVVGPSYFVEYLIKESPCTKSQASSCSLQSSDSVPVGLCKGS 240
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      181 ENTSKQYSLFKVTRASSQWVVGPSYFVEYLIKESPCTKSQASSCSLQSSDSVPVGLCKGS 240

Qy      241 LTRTHWEKFVSVTCDFFESQAPATGSENSAVNQKPTNLPKVEESQQKNTPPTDSPSKAGP 300
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      241 LTRTHWEKFVSVTCDFFESQAPATGSENSAVNQKPTNLPKVEESQQKNTPPTDSPSKAGP 300

Qy      301 RGSVQYLPDLDDKNSQEKGPQEAFPVHLDLTTNPQGETLDISFLFLEPMEEKLVVLPFPK 360
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      301 RGSVQYLPDLDDKNSQEKGPQEAFPVHLDLTTNPQGETLDISFLFLEPMEEKLVVLPFPK 360

Qy      361 EKARTAECPGPAQNASPLVLPP 382
            ||||||||||||||||||||||
Db      361 EKARTAECPGPAQNASPLVLPP 382
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